MARCH'S ADVANCED ORGANIC CHEMISTRY

REACTIONS, MECHANISMS, AND STRUCTURE

FIFTH EDITION

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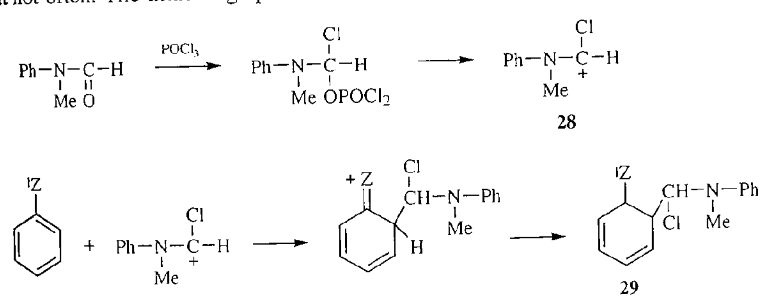
11-15 Formylation With Disubstituted Formamides

FORMYLATION OR FORMYL-DE-HYDROGENATION

The reaction with disubstituted formamides and phosphorus oxychloride, called the *Vilsmeier* or the *Vilsmeier–Haack reaction*,[317] is the most common method for the formylation of aromatic rings.[318] However, it is applicable only to active substrates, such as amines and phenols. An intramolecular version is also known.[319] Aromatic hydrocarbons and heterocycles can also be formylated, but only if they are much more active than benzene (e.g., azulenes, ferrocenes). Though *N*-phenyl-*N*-methylformamide is a common reagent, other arylalkyl amides and dialkyl amides are also used.[320] Phosgene ($COCl_2$) has been used in place of $POCl_3$. The reaction has also been carried out with other amides to give ketones (actually an example of **11-14**), but not often. The attacking species[321] is **28**,[322] and the mechanism is probably:



28 **29**

Compound **29** is unstable and easily hydrolyzes to the product. Either formation of **28** or the reaction of **28** with the substrate can be rate determining, depending on the reactivity of the substrate.[323]

When $(CF_3SO_2)_2O$ was used instead of $POCl_3$, the reaction was extended to some less-active compounds, including naphthalene and phenanthrene.[324]

OS **I**, 217; **III**, 98, **IV**, 331, 539, 831, 915.

11-16 Formylation with Zinc Cyanide and HCl:The Gatterman Reaction

FORMYLATION OR FORMYL-DE-HYDROGENATION

$$ArH + Zn(CN)_2 \xrightarrow{HCl} ArCH{=}NH_2^+ Cl^- \xrightarrow{H_2O} ArCHO$$

Formylation with $Zn(CN)_2$ and HCl is called the *Gatterman reaction*.[325] It can be applied to alkylbenzenes, phenols and their ethers, and many heterocyclic compounds. However, it cannot be applied to aromatic amines. In the original version of this reaction, the substrate was treated with HCN, HCl, and $ZnCl_2$, but the use of $Zn(CN)_2$ and HCl (HCN and $ZnCl_2$ are generated *in situ*) makes the reaction more